"TOPICAL BURN THERAPY COMPARING 'TOPICAL PVP + NEOSPORIN' AND AMNIOTIC MEMBRANE"

THESIS

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Rajendra Kumar)

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INTRODUCTION

INTRODUCTION

Thermal injury has been troubling mankind since he started using fire, and has caused great suffering to mankind physically, socially as well as economically.

Almost every minute of the day somewhere in the world at least one human being becomes a victim of burn. The magnitude of this problem is indicated by the fact that there are one lac cases of burns resulting in ten thousand deaths per year in India (Sinha, 1968). More so because burns are one of the necessary accompaniments of rapid progress including mechanization of life, where the susceptibility to burns has increased tremendously.

About 74% of all burn cases are domestic burns and 79% of all domestic burn involves women and children. Thermal burns are caused by application of heat to the body, the depth of the resulting burn injury is dependent on the intensity and duration of this heat application and conductivity of tissue involved. The most common source of heat are open flame and hot liquids. In addition, thermal injury is also frequently observed in patients who have been exposed to direct contact with hot metal.

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toxic chemicals or high voltage electricity. Industrial mishaps, civilian assults, laboratory accidents and inexpert application of agents used for medical purposes accounts for most of chemical burns in civilian population.

A principal difference between chemical and thermal injury is the length of time during which tissue changes continue, the chemical agents causes progressive damage until inactivated by the tissue, while thermal injury changes case shortly after removal of heat.

Various modes of local treatment have been suggested and used from time to time but the dilemma continues and the search for an ideal agent continues. In ancient times the emphasis in treatment of burn wound was local application of various medicinal products like resins and bitumen vineger, extract of plants, honey and bran, gum, goat hairs and other funny things as milk from mother who gave birth to a male child. Subsequently these local applicants changed to specific chemicals as tannic acid, silver nitrate, gention violet and petroleum gauze. With the advent of anti-microbials the emphasis turned to their local application as sulfanylon, sulphadizine cream etc.

Inspite of the local treatment, mortality and morbidity remains almost unchanged, which focussed the attention on three basic concepts regarding the local

problems of burn injury. (1) Burn injury provides a large raw area which causes a loss of large amount of water, electrolytes and plasma proteins, studies show that denuded skin increases the insensible loss up to 75 times and this also increases the heat loss.

(2) Large raw area with serum exudate provide huge culture plate for micro-organisms and lead to wound sepsis which is the basic problem in the management of burn wound. (3) The problem of pain caused by irritation of exposed nerve endings. To combat these problems, the coverage of burn wound is the only answer. The coverage of these raw area expeditiously still remains an integral but unsurmontable part of treatment.

Durn injury, various biological and synthetic covering materials have been used by various workers at different times. Different biological and synthetic coverings are homografts, skin hetrografts, skin collagen sheets and amniotic membrane, solid silicon, polymer membrane, cotton gauze fabrics, sprays, gels and laminets etc. But a perfect wound dressing is still a dream because covering materials although being good dressing materials have their limitations and disadvantages like subgraft suppuration, limited availability, high cost and cany potential risk of transmission of disease like hepatitis.

The management of burn wound sepsis is still a very challanging problem in terms of morbidity and mortality, inspite of the vast advancements in medical science and availability of various broad spectrum antibiotics. The avascular nature of burn tissue as a result of thrombosis of vessels limits the delivery of endogenic phagocytic cells and also decreases the efficacy of systemically administered antibiotics leading to propagation of infection. In addition to infection, wound maceration and pressure necrosis also favour microbial proliferation and impairs circulation. This local source of virulent organisms in the presence of lowered body resistance can alter the fragile balance between resistance and infection leading to frank septicaemia and death at any time (Liedberg, N.C.F., Reiss, E. and Artz, C.P., 1954).

Thus, it is necessary that treatment of local infection be given top priority and since systemic delivery of antibiotics is sub-optimal, more reliance is to be put on local methods of control of infection.

With this view, recently a combination of P.V.P. iodine and neosporin powder (Neomycin, Polymyxin B and Bactricin) are being tried in superficial and deep burns. Because of the inadequacy of presently used local application, we needed to re-examine a new combination of

locally applied chemotherapeutics/antibiotics and at the same time comparative study is made to assess the superiority of the dressing material.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

LOCAL CHEMOTHERAPEUTICS

Improvement in infusion therapy in burn has lead to a reduction in mortality due to shock, but the local management of burn wound still remains a very challenging problem in terms of morbidity and mortality.

Looking back at the ancient times various substances often exotic have been used. Thus 430 BC saw the use of tincture and extract of tea leaves by Chinese and Japanese, butter with rod orchro or bark of fig tree by Sushutra, boiled cow dung by Pappyrus (1500 BC), a mixture of gum, goat's hair and milk of a lady who has given birth to a son used by Egyptian (5th and 6th century), mixture of honey and bran for local application was used by Celsus of ancient Rome, various emolients preparations were used by Paulus of Aeigna (625 - 690 AD) and a mixture of white lead, oil of roses and wax had been used by Rhazes (580 - 920 AD).

Later during the 16th century and afterwards, upto 19th century Ambrose pone (1517-1590) suggested the use of ointment for the treatment of burn wounds.

Cleev's (1951) used five different complex preparations on different parts of the body area involved in burn.

David Cleghron (1792) used vinegar and chalk poultices

locally. Edward Kentish (1797) advocated pressure

bandages to relieve pain and to stop blister formations.

Marjolin (1797) described certain scars after burn known

to be cancer and Marjolin's ulcer. Sir James Earle (1799)

suggested the use of ice cold water and reported that it

acts as a good analgesic and prevents oedema formation.

William Clowe's (1544-1604) stands out in history as the first surgeon, since the middle ages to use the physical signs of burns; where the skin was burnt off, and parts were made raw and painful, to guide his local treatment. Hidamis (1607) in his book 'Decombustion' insisted that the classification of burn should be a guide for treatment, classifying burns into three degrees by external appearance; redness and blistering; withering of skin without charring, and eschar formation and charring. He warned against cooling burnt skin which hardens the tissues. In very deep burns, he made incisions to let the moisture escape, as otherwise gangrene and infection would supervene. So he was also the first to perform escharotomy. Wiseman (1676) observed that an organ which is burnt superficially is far more painful than deep. He too classified burns into four degrees like L. Heister (1682-1785) who also included time factor as a further

diagnostic aid. In 1814 Boyer classified burns into three degrees (1) Erythema, (2) Blister leading to superficial ulcer, and (3) Charring of skin and eschar formation. Dupytren's (1832), a famous French surgeon classified burn into five degrees according to the depth of involved tissues.

- Erythema or superficial ecchymosis which blanches on pressure.
- Cutaneous inflammation with loss of epidermis and the development of vesicles filled with serum.
- 3. The destruction of a portion of the papillary body.
- 4. The disorganisation of whole dermis upto the subcutaneous cellular tissue, and
- 5. The formation of eschar.

He also described the four periods during natural course of burn injury (1) Period of irritation, (2) Period of inflammation, (3) Period of suppuration, and (4) Period of exhaustion. In addition, he also noted about the gastro-intestinal tract haemorrhage in burn cases. Later Curling (1842) recognised gastric and duodenal ulcer as a cause of this gastro-intestinal haemorrhage. He also suggested the use of saline bath for local wound management.

As far the local management is concerned,
Passowant (1856) suggested the use of saline baths,
Hobra (1861) treated burn cases in warm water bath,
believing that Dupytren's last degree of burn were of
academic interest only and he returned to the three
degree classification which defined the 3 stages as,
erythema with swelling, with pain, blistering with
bacterial haemorrhage and eschar devoid of sensation.
(Hobra (1866).

The dry method of dressing was the principal method between 1863 - 1868. Syme (1834) in his principles of surgery stated that this form of therapy had almost superseded the filthy and useless application of carson oil and linimentom aquae calcis.

The 19th and 20th centuries introduced two new principles in the local treatment of burns (1) skin grafting (Pollock, 1971) and (2) open treatment (Coopland, A., 1887), Stocher, 1894 and Raid, 1898) in addition to newer local applicants. However, Bonisson had used open treatment about 400 years back and hence this was not an entirely new approach. Lusgarten (1871) suggested and Wiltms (1901) carried out excision of burn tissue for the first time but he never grafted the excised area. Jauzehoric (1968) revived the idea of excision of burnt tissue and immediate skin grafting, thus adding a footnote to a contemporary principle of early tangential excision and early grafting.

Lister (1868-1885) used 2.5 percent carbolic acid topically, but it was soon discarded because of its toxicity, causing local gangrene and after absorption through the burnt area causing systemic toxicity i.e. muscle twitchings, weakness, excitement, nausea, vomiting, delerium and hypotension.

An important period called the saline wet dressing antiseptic era extended between 1885 to 1910. Wet dressing with sodium bicarbonate were first applied - followed by solution of picric acid or boric acid advocated by Oppenheimer (1906). A. Maclennen (1903) and E.J. Elliot (1906) described picric acid poisoning following its use on dressings applied to burns. Picric acid induces tachycardia, nausea, vomiting, diarrhoea, moderate fever disoria, renal insufficiency, discoloured urine, stupor, coma and collapse. The systemic absorption of boric acid is known to be followed by rashes with desquamation of skin, restlessness, confusion and weakness, hypothermia, hypotension, tachycardia and renal injury.

rom 1910 to 1926 wax containing 250 mg% of beta naphthol was applied at a temperature of 50°C to 60°C. Beta naphthol causes extreme hepato-renal damage with convulsive seizures and even death. Dexitson (1894-1933) advocated the use of tannic acid application on burn surfaces in 1925 at Henry ford hospital he claimed that this agent decreases the fluid loss, relieves the pain

and produces a clean scar. Later on, Maclure of the same hospital in 1944 described it as a hepato-toxic agent and attributed many deaths of its toxicity. Aldridge (1933) advised the use of gention violet as an escharolytic agent on burn surfaces.

At the turn of the 19th century, the emphasis was to avoid infection and with the advent of the 20th century, a better understanding of the pathophysiology of burns elucidated causes and indicated methods of better systemic treatment of burns, and counteracting shock. Reiss (1890) and Tommaroli (1897) introduced the systemic treatment of shock by intravenous saline transfusion in severely burnt patients. This treatment of shock in the 4th decade of this century has now become a standardised procedure especially after the remarkable work of Davidson (1926). Underhill (1930) and Bdalock (1931).

This was the turning point and since the mid 20th century there has been an increased understanding of the metabolic, nutritional, immunological and wound healing processes improving the overall management of burn patients. But the local treatment still leaves a lot to be learned.

In 1942, Allen and Koch used petroleum gauze piece locally with strict immobilization, this type of occlusive dressing were used in army hospitals during world war II.

Wallace of Edinburgh (1949) in England and Pulaki, Artz and Blooker (1950) in U.S.A. reintroduced the exposure method of burn wound, later on other surgeons accepted the same method with a view that development of a crust provides physiological covering to burn wound, thus reducing the harmful effects of raw area.

Work of Leidberg, Reiss and Artz (1953) indicated septicaemiae as a primary cause of death in burns as a result of uncontrolled local growth and staphylocci as the main organism. With the availability of antibacterial agents against gram positive organisms, pseudomonas emerged as the major organism responsible for sepsis and death. This lead other workers to find out newer antibacterial agents effective against gram negative organisms and other microbials which can penetrate burn surface and thus minimize the growth of such microbials. Since then various antimicrobials were tried and some are still in use, e.g. 0.5% silver nitrate (Moyer, 1960), Mefanid or sulphamylon (Moncrief, 1974), Silver sulphadiazine (Fox, Jr. and others, 1969), Cerium nitrate (Williams, W. Monafo, Som N. Tandon, 1975), Cerium nitrate and silver sulphadiazine (Fox, C.L. Jr. and others, 1975), but these agents are effective mainly in controlling the microbial population, not erradicating bacteria from the wound. It is stated that from an average of 10 microorganisms per gram of tissues, reduction to 104 per gram

of tissue occurs as a result of these agents (Artz, C.P. et al. 1979). Besides this limited local activity, these agents also have some advantages and disadvantages.

patients, but this causes metal toxicity, depletion of body salt and necrobiosis. It was soon replaced by silver sulphadiazine because it has dangerous side-effects. Silver sulphadiazine has the following advantages, (1) it readily penetrates eschar, (2) Eschar does not adhere to dressing, (3) this drug inhibits nearly all pathogenic bacteria and fungi and exerts prominent action against pseudomonas (Rosenkraz, 1972), but at the same time it also has some disadvantages - (1) It is absorbed through the raw surface causing crystalluria, (2) Bacterial resistance to these drugs which is plasmid mediated, (3) Adverse reactions including burning, rashes and itching, (4) It is also a very costly drug, and (5) Difficulty in daily application on burn surfaces.

Thermal injury results in striking anatomic, metabolic and physiological disturbances which prejudice survival of burn patients. The main cause of morbidity and mortality in these patients is toxiaemia due to absorption of toxins from injured surface of burn invaded by micro-organism. So the new concept of burn cure is restoration of impaired barrier by using various covering materials as skin substitutes.

BIOLOGICAL DRESSINGS

Autogenous skin grafting is the best dressing material amongst all suggested till this time, but it has its own limitations in the form of limited supply, unfitness of the already shocked patient for surgical procedure involved in skin grafting and refusal of patient or his attendant on religious, sentimental or economic grounds. To overcome this problem, various temporary biological and synthetic covering materials for short periods till the healing of wound has taken place or permanent in place of lost skin has been suggested by different workers.

Various materials used for skin substitutes are listed below.

1. Biological -

- a) Human allograft (Homograft)
 - living donor
 - cadaver donor fresh
 - cadaver donor frozen
 - Amniotic membrane.
- b) Xenograft (Hetrograft)
 - Living donor fresh
 - frozen, radiated or dried.
- c) Tissue derivatives
 - Collagen sheet fabrics or sponges,
 - Bioplast fibrin.

2. Synthetics -

- Solid silicon, polymer membrane, other plastics, Microporous material.

3. Composite materials -

- Surface membrane (Silicone, microporous trydron).

 Adherent substrate -
- Collagen, cotton gauze, synthetic polymer sponge, vetour, flecking or febric.

Homograft:

Pallock (1871), Cirdner (1881) and Shede (1881) were pioneers in this field. Cirdner (1881) treated a lightening burn with the skin from a suicide victim, Shede (1881) used skin from amputation specimen as well as from a cadaver the limit of 24 hours. Ivunova (1890) stressed the use of foetal skin as a homograft on burn surface because of its more energetic vitality.

In the middle of the present century, Dogo (1952) of Italy, noted the usefulness of cadaver skin obtained in a viable state, it was useful where it was possible to preserve the tissue till the time of application. He measured skin viability by determining the tissue oxygen taken up in the Warburg apparatus, the skin was preserved at 3°C in physiological solution. The oxygen consumption of cadaver skin was noted to be unaffected upto 16 hours after death.

Brown (1952) used allografts as emergency dressings for burn. He stated that skin may be removed even a day after death, if the cadaver has been placed in cold storage. Eade (1958) and Morris (1966) observed that the homograft have organisational and debridemental effects on healing.

Miller (1967) had reported that healed epidermis alteration in the architecture, and the dermis contains bedematous connective tissue in 2nd degree burn, where homograft was not used, when homograft was used, the healed epidermis shows normal architecture with reorganizable basal layer and normal collagen bodies in the dermis. James O' Neil Jr. (1967) used temporary homograft coverage over open wounds including 2nd and third burns, such coverage was a distinct benefit following eschar separation in burn injury. Sharma et al (1978) reported the same results. Allograft skin besides being a satisfactory biological dressing, have their own limitations. Cadavers suitable for skin donation are limited in number. Bexter (1970) has estimated six physician hours and hospital cost of \$ 225, per patient treated by the use of cadaver homograft.

Amniotic Membrane -

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The quest for a cheap, painless and easily available biological dressing having most of the

properties of the ideal skin substitute led the people to use amniotic membrane.

The amnion is the inner foetal membrane, its inner surface is in contact with the amniotic fluid and foetus, its outer surface is separated from decidua of uterus by chorion. It has the following parts -

- 1. Placental amnion lines the inner aspect of placenta.
- 2. Reflected amnion lines rest of the amnion.
- 3. Dependent amnion overlies the internal os of cervix.

Histologically it has five layers - (1) epithelium, (2) basement membrane, (3) composite layer, (4) fibroblastic layer, (5) sponge layer. The thickness of the membrane is variable due to variable amount of mucin and fluid in spongy layer. Normally the thickness is 1/50 to 1/2 mm which can be increased to as much as 2 - 5 mm.

The first person to report the attempt of grafting pieces of lining of amniotic sac on granulating wound was John Staiger Davis, a medical student in 1910 at John Hoffkins University. Sabella (1913) used amniotic membrane on raw surface caused by burn and ulceration. He observed reduced pain, rapid epithelialization and absence of infection after application of amniotic membrane. Kubanyi (1941-48) reported the use of amniotic membrane in burns, traumatic loss of skin and to prevent intraabdominal adhesions. Pinkerton (1942) reported the use

of amnioplastin to prevent adhesion between flexor tendon and their sheets. Hensen (1950) used amniotic membrane in the management of non-healing ulcer of skin and compared granulation tissue to that of other methods as plaster of paris. Jullian A. Sterling (1956) successfully used the amniotic membrane over old infected flame burns.

Pigeon (1960) observed the foll wing effects in burn patients dressed with amniotic membrane.

A. Immediate effects:

- Pain relieved at once after application and no further analgesics were needed.
- Antibiotics were used only after development of complications.
- 3. The dressing were generally found dry.
- 4. Healing of wound was rapid and complete.

B. Delayed effects:

- 1. No discolouration was observed.
- 2. Minimal scar tissue.
- 3. No contracture were observed.

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4. He also stated that amniotic membrane undergoes changes similar to that of cornified cells.

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Trelford and associates (1975) reported the use of amnion alone in full thickness fresh surgical wounds leading to decrease in pain, fluid loss and secondary infection and hence decrease in hospital stay.

Bose, B. (1979) recently reported the use of amniotic membrane over burn wounds specially in developing countries like India.

Xenograft -

The use of hetrologous tissue as a temporary dressings for full thickness skin defects was largely a result of the difficulty of obtaining adequate amounts of homografts. Brown (1954) and Jevis (1976) have shown that adherence of allograft and xenograft is similar. Hetrografts provides a readily available, easily stored and sterilized dressing in contrast to homografts.

canine skin had been used by Snitzer et al (1960) in treatment of tissue injury. Bromberg, B.E. et al (1965) and Elliot and Hoehn (1973) have used pig skin. Variable results have been reported ranging from early re-epithelisation to conversion of full thickness skin loss, with porcine xenograft coverage of donor sites and partial thickness burns. Salisbury (1973) has reported that incorporation of xenograft tissues on healing donor sites occurs in 35 percent of cases. There appears to be no significant difference in the effectiveness of fresh

compared with fresh frozen or frozen, irradiated procin skin.

The most striking advantages with procine xenograft is that of immediate and lasting pain relief. Xenograft has most of the properties of ideal skin substitute. A viable xenograft is antigenic but dead is not. The major problem is the propensity to digestion by wound collagenase and subsequent infection.

Collagen Sheets - Collagen is a fibrous protein present in many animal tissues, like skin, muscles and bone. Its structure and immunologic chemistry are well characterized and antigenicity can be altered. It possesses a haemostatic effect and when implanted in living animals in pure form, no antigenic reaction is seen. Collagen sheets are derived from serous, subserous layer of freshly slaughtered cattle intestine, and these are available in 4" x 6" size packed in cylindrical glass tubes containing ethelene oxide which act as sterilizing agent.

Sinha (1972), Shankar (1973) and Gupta et al (1976) used collagen sheets as primary cover material in the management of burns. Gupta and Chaturvedi (1974) used it to cover donor area. Thuksal and Gupta (1976) have used collagen material in repair of bernia and to cover surgical defects. Ehlan (1978) used collagen sheets as biological dressing in 35 patients and reported it in

prevention of infection and rate of healing. Jain et al (1976) reported similar findings.

The beneficial effect of collagen sheets include:

(1) prevention of air born infection, (2) minimizing

fluid loss, and (3) promoting formation of health and

pink granulation tissue. But it is an expensive material

and is not available at every centre.

Synthetic materials - The problems associated with biological materials provided an impetus to search for synthetic materials, with ideal properties, or for skin prosthesis. Many of these materials adhere by entrapment of coagulum in the interestices of the material.

widely utilized because of their permeability to water (Travis, M.J. et al, 1978). Kornbeg et al (1977) have used this silicon membrane banded to cotton gauze for temporary skin substitution, but it lacks elasticity and creates non-uniform pattern of adherence. Other materials - polyurethane, Polyvinyl chloride polymers, nylon mesh, decron velours, amino acid film and Polyhydroxyethyl-Methacrylate, have been introduced, all of which have ideal properties of water permeability, elasticity and variable degree of adherence to the wound (James et al, 1973; Lamkey et al, 1977; Towsend, 1977), but the infection is a major liability when used with latter wounds

(Zachary et al, 1982), another drawback to dressing applied as a foam particularly Polyurethane appears to be the incorporation of the agent with the cells of the healing wound and subsequent foreign body giant cell reaction (Salisbury, R.E., et al. 1979). In an apparent departure from derived properties of wound covering, a gas permeable dressing employing a hydrocolloid polymer complex has been demonstrated in a well designed clinical trial to significantly promote partial thickness wound and patient comfort (Madden, M.R., et al, 1984). This study suggests that synthetic would dressing may justify their greater expence and seem as a model for evaluation of all similar dressings. Another major advance in burn wound closure has been the development of skin substitute which potentially can be incorporated directly into the healing of wound. Three major elements of artificial skin are epidermal surface (Tsoa, M.L. et al, 1982 and O'Connor, N.E. et al, 1984), underlying matrix (Bell, E. et al, 1981 and Yannus, I.V. et al. 1982) and human epidermal cells in culture with loss of HLA - DR antigen expression (Elsinger et al, 1979), but these artificial skin substitutes are still in phase of trial and available in limited centres in developed countries.

<u>Disadvantages of biological dressings</u> - Inspite of being the best dressing material for burn wounds,

energy will be a process of the formation of the process of the control of the co

biological dressings have certain disadvantages in the form of

- 1. Sub-graft suppuration,
- 2. High cost,
- 3. Lyophilized allograft skin shows less adherence to the wound and is of sufficient thickness, undergoes dermal, epidermal separation after application to the wound with subsequent dessication of exposed dermis.
- 4. Potential transmission of disease like hepatitis in case of cutaneous allograft.

NEWER TOPICAL AGENTS

The problem of burn wound sepsis is now becoming increasingly important, because the systemic delivery of antibiotics at burn wound site is suboptimal. There has been an introduction of many treatment modalities directed at this problem, e.g. Topical antimicrobial oint. (Fox, C.L. Jr., Rapport, B.W. and Stanford, W., 1969), early surgery i.e. escharotomy or skin grafting (Burke, J.F., Bondoc, C.C. and Quinby, W.C., 1974) or amniotic membrane application (Bose, B., 1979).

Topical agents should play an important role in the management of burn injury. Since the availability of various topical agents, the topical burn therapy has contributed substantially to the reduction in sepsis to fight against infection. A number of techniques with topical agents have been evolved in mid 1960s, that have substantially decreased the incidence of burn wound sepsis, but each has its own advantages and disadvantages.

Amongst the many topical agents used are - silver nitrate, where the silver ions are immediately precipitated and are responsible for the discolouration of the local area. This agent also leads to Na⁺, K⁺ and Cl⁻ deficits and alkalosis (Mayer, 1960). Silver sulphadizine (S.S.D.) which exerts a prominent antibacterial action against pseudomonas but poorly penetrates eschar (Rosenkraz, 1972). Sulfamylon, which is freely soluble and readily diffusible through the eschar (Leidburg, Moncrief and Mason, 1960), but since sulfamylon is a potent inhibitor of carbonic anhydrase, it may induce acid base dearrangements leading to acidosis.

Recently topical application of PVP, a complex of iodine with polyvinyl, pyrrolidone (M.de.Knoch, 1985) has been used, which destroys both gram positive and gram negative bacterial cells.

The excellent antibacterial properties of PVP make it particularly suitable as a topical agent on burn wound. However, like so many other topical agents, pintments, it lacks the ability to actively penetrate

burnt tissue, and this distracts it considerably from its usefulness in treatment of burns.

alongwith aserbine (Knock, D.M., 1985). P.V.P. is effective against a wide range of gram positive and gram negative bacteria as well as some fungi, but it causes pain on application and excessive drying of eschar (Schwarts, Shires and Spancer, 1988). Prolonged treatment with povidone iodine does not have any effect over thyroid glands (Balogh, D., Baner, M. and Riccabone, G., 1984).

Neomycin powder (Wellcome & Burrough's) which can also be used locally has the following ingredients, i.e. Neomycin sulphate, Zinc bactricin and polymycin B.

Neomycin was isolated from streptomyces fradial in 1949 and is effective against gram negative species that are highly sensitive, E. coli, enterobactor and proteus vulgaris. Gram negative micro-organism which can be inhibited by neomycin include Staphylococcus aureus, streptococcus faecalis and mycobacterium tuberculosis. The hypersensitivity reaction is primary skin rashes in 6-8% of patients. The most important toxic effect of neomycin is nephrotoxicity (Kurian et al. 1960; Lert and Sherlock, 1960 and Berk and Caulinan, 1970).

Polymyxin B discovered in 1947 is a bactericidal. polypeptides derived from spore forming rods, found in soil by various strains of bacillus polymyxa. The antibacterial effect of polymyxin is unique in that, it is directed at bacterial cell membrane and induces major defects in permeability of bacterial cell (Gale et al, 1972; Corcoran and Huhan, 1931). The sensitivity to polymyxin B is apparantly related to the phospholipid content of the cell wall membrane complex (Brown and Wood, 1972). The antibacterial activity of polymyxin B is restricted to gram negative bacteria including Pseudomonas aeruginosa, E. coli, Klebsiella, Salmonella, Partousella, Bredetella and Shigella (Kucers and Benett, 1975). Because of extremely nephrotoxicity (Rayan, K.J. et al, 1969; Price, D.J.E. et al, 1970; Koch-Weser, et al, 1970; Renold et al, 1975, and Flick and Cluff, 1976) associated with parentral use of this drug is now rarely used except orally for prophylaxis, otic and ophthalmic and topical gram negative infection (Enno, et al, 1978; Gurwith et al, 1979). Polymyxin B applied to intact or denuded skin or mucus membrane produces no systemic reaction because of almost complete lack of absorption of the antibiotic from these sites. Hypersensitivity is uncommon.

Bacitracin is an antibiotic produced by the tracy I strain of bacillus subtalis. The history, property and uses of bacitracin have been reviewed by

Meleney and Johnson (1949). This peptide antibiotic inhibits cell wall synthesis (Strominger, 1973). It is bactericidal in vitro against a variety of gram positive cocci and bacilli, Neisseria, H. influenza and T.palledum, Actinomycoses, Furobacterium, Enterobacteriaces, Pseudomonas, Candida Torule and Nocardia are resistant (Merk, A., Samdo and Gerald, L., Mondell, in Goodman & Gillman, IV Ed.). Because of its high rate of nephrotoxic reactions that followed its systemic use, it is now limited to topical application. It is often combined with polymyxin B and neomycin to provide broad spectrum coverage. Little systemic absorption occurs from topical application and allergic reactions are rare (Goodman and Gillman, 1975; Kucers and Benett, 1975).

The combination of drug treatment utilizing PVP + Neosporin powder may act as complementary to each other (Sinha et al. 1988).

Clinical and investigatory tools of assessment of burn wound sepsis among others are surface culture and sensitivity report, regarding the type of infectious organism and quantitative estimation of these organisms indicating the degree of infection.

Burn wound biopsy provides three parameters for assessment of infection.

- 1. The first quantitative bacteriology.
- 2. The second is qualitative bacteriology.
- 3. The third parameter of burn wound biopsy is 'histologic', where perilymphatic, perivascular and intraluminal accumulation of bacteria prove without doubt invasive burn wound infection (Krupp, S., Baechler, M. and Bille, J., 1985).

In the qualitative bacteriology, immediate gram staining shows the presence of bacteria and the identification of bacteria from wound biopsies provides precise identification. The organisms which have been recovered from culture of wound swabs and wound biopsies are as follows:

- A. Gram negative bacilli Enterobacter spp., Klebsielle spp.

 E. coli, Pseudomonas, Aeroginosa etc.
- B. Gram positive bacilli Enterococci, Staph-epidermis,
 Staph. aureus, Streptococcus.
- C. Other opportunistic infections. Fungal e.g. Candida spp, yeast and viral infection.

It should be kept in mind that the microbial etiology of burn wounds of the patients could at any burn unit leeds changing with time and attentions in the flora occur as a series of mini-epidemics with a succession of predominant organism.

In view of the organism found locally, a topical anti-microbial with a total spectrum coverage and minimal side effects and at the same time easy to apply with minimal strain on nursing personnel is desirable. PVP with Neosporin may fill this gap which has been unfilled to date. The nearest to this appears to be amniotic membrane but it too has some disadvantages especially sub-graft suppuration.

This study would examine the efficacy of PVP and neosporin powder in the above light especially in comparison to amniotic membrane application.

MATERIAL AND METHODS

MATERIAL AND METHODS

The present study has been conducted at M.L.B.

Medical College, Jhansi from April 1990 to April 1991.

Three groups of patients with superficial, deep and mixed (superficial + deep burn) were included in this study. They were subdivided into two sub-groups matched by age and percentage of burn. One sub-group was treated with a combination of Povidone Iodine lotion + Neosporine Powder and other by application of Amniotic membrane.

Material

Betadine lotion - is available as 10% Povidone-Iodine providing 1% available Iodine.

Neosporin Powder (Wellcome and Burrough) - It is available in powder form, 10 gm pack are available in market. This powder contains the following three ingredients per gram.

- 1. Polymyxin B sulphate 500 U.B.P. of Polymyxin B sulphate.
- 2. Zinc Bacitracin 400 U.B.P. of zinc bacitracin.
- 3. Neomycin sulphate 3400 U.B.P. of neomycin sulphate.

Neosporin powder is sprinkled over the burn area till a uniform coating of powder is obtained.

Amniotic membranes

Placentae from vaginal deliveries and emergency and elective caesarian section were collected by sterile technique. Placentae with intact membrane was taken directly in a clean tray and was washed thoroughly in running tap water to remove blood and mucoid material.

another tray filled with water. The amniotic membrane was separated from chorion and placentae, gently starting from the periphery upto the base of umblical cord. The separated membrane was cut at the base of umblical cord.

The separated membrane was then transferred in a sterile container filled with sterile normal saline. The remaining clots were removed from its surface and washed further with sterile normal saline solution 3-4 times. Now the obtained membrane is transparent, tensile, shining and stronge which can cover a wide surface area.

The obtained membrane were either applied immediately or can be preserved in sterile normal saline (400 cc) treated with 10 lacs unit of crystalline penicillin, 1 gm. of streptomycin sulphate and 50 ml of liquid metrogyl and kept at 4°C in refrigerator till the time of application.

Selection of cases -

All the cases with superficial, deep and mixed (superficial + deep) burns, who came to the emergency or out patient department of this hospital were included in this study irrespective of their age, sex, socio-economic status, contamination and mode of injury.

Method of study -

The selected cases were subjected to a detailed history and physical examination which were recorded on the following lines.

History

Introduction:

Name

Age

Sex

Urban/Rural

Occupation

Address

Date of admission

Date of discharge

Time of healing.

Regarding the burn accident -

Date and time of burn (Duration of burn)

Place of accident and nature of work at the time of accident.

Cause of burn

Prior treatment (if any)

Symptoms

Physical examination -

General examination:

General condition

Pulse

Blood Pressure

Temperature

Respiration

Hydration.

Local examination -

(a) Percentage of burn. It was calculated by Wallace's rule of urine, in the adult and by & Brown chart in children.

(b) Depth of burn - Superficial / Deep / Mixed
 (Superficial + deep).

Estimation of depth of burn -

A hypodermic needle was used to discern the pain sensation. The area with increased sensibility was considered to be superficial or partial thickness burn, the deep area had markedly reduced or absent pain sensation. This was also confirmed by pulling out a hair from surface. In the 3rd degree or deep burn, hair could be pulled out easily and painlessly. The later test is of value in borderline cases of 2nd degree burn.

The state of the s

In addition, help of following criteria was also sought.

Appearance of burn area	Pain sensation
Erythematous	Painful and hyperaesthetic.
Blisters with reddened base and moisture.	Painful and hyperaesthetic.
Blistered with blanched base and moisture.	Painful, hyperaesthetic or anaesthetic at places.
Leathery pale or pearly white or charred dry.	Painless and anaesthetic.
	Erythematous Blisters with reddened base and moisture. Blistered with blanched base and moisture. Leathery pale or pearly white or

The I and II(a) were included as superficial and II(b) and IIIrd were included as deep burn.

(c) Contamination of wound -

Apparantly clean : No contamination of foreign body, clean, intact blisters.

Mild contamination: Slight contamination, ruptured blisters, open wounds.

Gross contamination: Heavy contamination with dirty cloth, foreign body, dust and pus etc.

(d) <u>Area involved</u> - Diagramation in anterior, posterior and lateral view (Shown in attached proforma) was done.

Resuscitation and general management :

Patients were resuscitated prior to application of betadine with neomycin powder or amniotic membrane, by I/V fluid, blood, plasma, infusion, analgesic, antibiotics and tetanus prophylaxis, according to the need of patients.

Local management of wound :

The shall traver for the

Preparation of burn surface - A swab from burn surface was taken for culture sensitivity test. Necessary sedation was given to the patient. A gentle but thorough debridement of wound was done by removing necrosed skin and blisters. The area was again tested for degree of burn. Then the wound was cleaned with sterile normal saline thoroughly.

Application of FVP + Neosporin Powder in superficial burns - The application was started by cleaning with saline, then sprinkling a uniform layer of neosporin powder on burn surface. Over this the solution of FVP with 1% available iodine was sprayed uniformly. Thus completely soaking with powder. A further layer of powder was applied to form a crust. On first day three such applications were carried out without removing the previously applied layers. On the second day, the application was reduced to two and from the third day onwards, this application was limited to those areas from which the crust was either separated or cracked.

Subsequently, these areas showing discharge with infection were subjected to twice daily applications each time after removal.

Method of subescharal injections (Escharolysis) of Betadine lotion in deep burn patients:

In patients with deep burns, the PVP solution (1% available iodine) was diluted with three equal volumes of normal saline and was injected at multiple sites in the subescharal plain as a 0.25% solution. Each injection prick received 0.5 ml of this solution. This injection was started on the third post burn day and repeated twice weekly until escharolysis was completed. The injections amounts to about 0.5 ml per square inch of burn surface every time. In patients with more than 50% deep burns, injections was restricted to three injections at 72 hours, 7th day and 14th day, basically to limit the amount of PVP injected.

Application of amniotic membrane -

The membrane with bad odour and colour changes were discarded. It was streched open and then applied over cleaned burn to upto about one inch beyond the margins. The air bubbles between membrane and wound area were removed. The patient was instructed not to move the pack until the membrane became adherent and relatively dry. It was left as such without any dressing except in

children and unco-operative patients where the dressing was applied to retain the membrane.

Assessment of the cases -

The assessment of the result was done by interview with patients, examination visits and investigations.

Interviews - The patients was asked about -

- 1. Pain and discomfort (mild, moderate, severe),
- 2. Fever,
- Any evidence of allergy as "Itching, rashes, nausea, and vomiting.

Local examination - Observation for following was done -

- Presence of discharge and/or soakage.
- 2. Appearance of burn area covered by betadine, neosporin powder and amniotic membrane.
- 3. Collection of pus under dressing, if the pus was localized, it was cleaned and thoroughly washed.

 Fresh application of dressing was done. A pus swab was taken for culture and sensitivity test.
- 4. Formation of crust.
- 5. Formation of healthy granulation tissue.
- 6. Appearance and duration of eschar.
- 7. Assessment of epithelization and healing of wound.

WORKING PROFORMA

Name

Age

Sex

Address

Date of burn

Date of primary treatment:

Date and time of admi- : ssion (interval between burn and admission)

: Superficial: Percentage of burn

Deep

Mixed

Nature of burn

Method of sustaining

primary treatment given :
prior to admission

Lat.

Ant.

Post.







Clinical examination -

General condition

Pulse rate :

Blood pressure :

Respiratory rate

Temperature .

Urine output since burn

Infection

Eschar

Type of burn : Superficial

Deep (Eschar)

Treatment given

- Fluids :

- Blood :

- Analgesics

- Antibiotics

- Ryle's tube aspiration :

(RTA)

- Catheterization

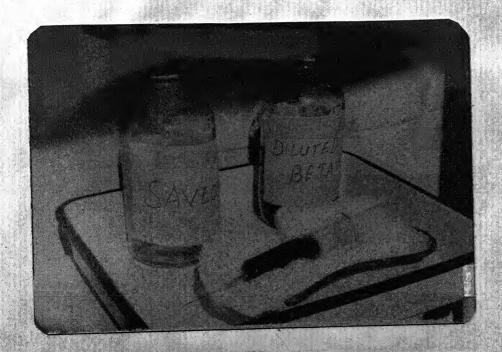
Topical microbicidal

	I Povidone iodine Ne Super- ficial (PVP+N)	II Silver Sulpha- dizine (SSD)	Amniotic membrane
No.of applications			19
Ist day		P .	
2nd day	-		
After 48 hours			
Evaluation :			
Urine output/24 hrs.			
Infection -			
- Local			
- Toxaemia/ Septicaemia			
Eschar separation:			
- Started (days)			
<pre>- Completion (Separation)</pre>			
Surface culture and sensitivity report			
Qualitative :			
- Pre-treatment			
- 48 hours			
- 7 days		-	
After eschar separation		1994	
Quantitative :			
_ 48 hours			
- 7 days			
Time of complete healing (days)			
- With grafting			
- Without graftin	g i		
Mortality			



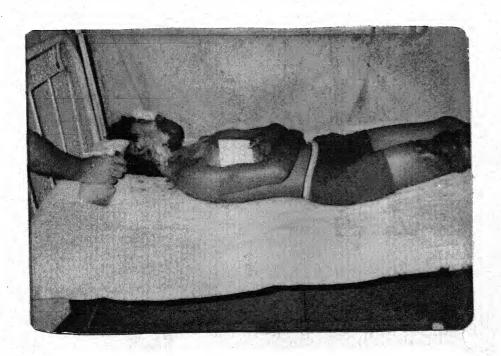
Photograph - A

Showing materials as Betadine lotion, Savlon, lotion spray machine and Neosporin powder in a tray.



Photograph - B

Showing materials for subescharal injections of diluted Betadine with syringe (20 ml.) and Needle (No. 18, 142 inch length).

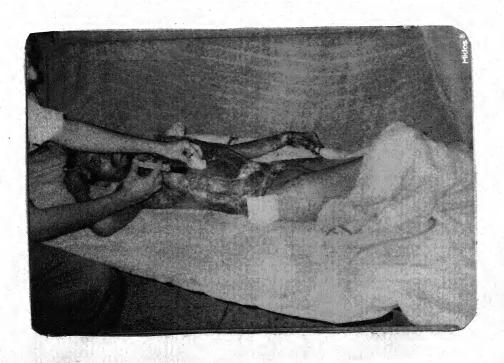


<u>Photograph - C</u>
Showing method of Betadine spray by spraying machine.



Photograph - D

Showing method of sprinkling of Neosporin powder.



Photograph = E
Showing method of sub-escharal
injections.



Photograph - F
Showing method of Amniotic membrane
separation.

OBSERVATIONS

and the first because of spec-

OBSERVATIONS

The present study consists of 114 patients of superficial, deep and mixed (in which both superficial and deep burns are present) burns admitted to Emergency ward or out patient department of M.L.B. Medical College, Jhansi, from April 1990 to April 1991. These patients belonged to different social status and were of either sex. These patients were of an age group ranging from 2 years to 50 years and percentage of burn ranging from 8% to more than 60%.

Out of 114 patients, three groups of patients were grouped as follows - 47 patients with superficial burns in Ist group, 20 patients with deep burns in IInd group and 47 patients with mixed burns (superficial & deep burns) in group III. Each group was sub-divided into two sub-groups. One sub-group was treated with a combination of Povidone Iodine lotion + Neosporin Powder (PVP + N) and another by application of Amniotic membrane (AM).

Total male patients were 53 (46.5%) and female patients were 61 (53.33%) (Table II). Maximum incidence of burn was in 11-30 years of age group; in both sexes.

33 male patients out of 53, i.e. 28.1% and 46 female patients out of 61, i.e. 40.5% were in this age group (Table II).

Incidence of superficial burns (47 patients, i.e. 41.3%) and mixed burns (47 patients i.e. 41.3%) was equal. Deep burns were less common (20 patients, i.e. 17.6%) (Table III).

Out of 114 patients, 76 were taken up for treatment with PVP solution + Neosporin Powder and 38 treated with application of amniotic membrane (Table IV).

All groups of patients (superficial, deep and mixed) showed lesser incidence of growth of organism both at 7th and 18th day when treated with PVP + N as compared to amniptic membrane (Table V).

Quantitatively, the percentage of patients presenting a bacterial count below $10^5/\mathrm{cm}^2$ was markedly better in PVP + N treated patients with superficial, deep and mixed burns as opposed to amniotic membrane. There was lesser percentage of patients presenting a bacterial count more than $10^5/\mathrm{cm}^2$ in PVP + N treated patients as compared to amniotic membrane treated patients (Table VI).

As for rate of healing, most of the superficial burn patients, when treated with PVP + N, showed complete

healing with 15 days (28 patients out of 31), while amniotic membrane sub-group, majority healed within 30 days, a substantial number of wound took 45 days to heal (7 patients out of 16). Deep burn patients treated with PVP + N healed within 45 days and few wounds took more than 45 days (3 patients out of 20). While amniotic membrane treated patients showed complete healing within 45 days (percentage of burn was less in this sub-group as compared to sub-group of PVP + N). Group of mixed burn patients treated with PVP + N showed complete healing within 45 days. Out of 32 patients in this sub-group, 9 took more than 60 days (percentage of burn varies between 40 - 60%). Patients of this group treated with amniotic membrane took 45 days for complete healing, while substantial number of patients took more than 60 days (5 patients out of 15 and percentage of burn varies between 20 - 40%) (Table VII a & b).

Healing was better and speedy when Povidone iodine lotion + Neosporin powder was applied.

TABLE I

Age incidence.

Sl.	Age group	No. of patients	Percentage
1.	0 - 10	20	17.6
2.	11 - 20	30	26.4
3.	21 - 30	48	42.2
4.	31 - 40	12	10.6
5.	41 - 50	4	3.6
6.	51 - 60		
7.	7 60		<u>-</u>
Tota	7	114	100.0
Tota			j. 59

TABLE - II
Showing sex distribution in different age-groups.

Sl.	λαο	aroun	M	ale	Fen	nale
.cM	Age	group	No.	%	No.	%
1.	0	- 10	14	12.3	6	5.3
2.	11	- 20	10	8.8	20	17.6
3.	21	- 30	22	19.3	26	22.9
4.	31	- 40	6	5.3	6	5.3
5.	41	- 50	1	0.9	3	2.7
6.	51	- 60	- -	_	-	-
7.	7	60				
Total		w.	53	46.5%	61	53.5%

TABLE - III
Showing percentage and depth of burn.

Sl.	Percentage of burn	S	Depth of D	burn M	Total
1.	0 - 10	21	. 8	4	33
2.	10 - 20	12	4	5	21
3.	20 - 30	8	5	11	24
4.	30 - 40	4	1	11	16
5.	40 - 50	1	2	8	11
6.	50 - 60	1	-	4	5
7.	7 60			4	4
Total	4	47	20	47	114

S = Superficial burn

D = Deep burn

M = Mixed burn (both superficial & deep burn).

TABLE - IV
Showing treatment regimes.

Sl.	Percentage		PVP + N		Amni	otic Mem	brane
No.	of burn	S	D	M	S	D	М
		*				_	×
1.	0 - 10	14	5		7	3	4
2.	10 - 20	9	3	2	3	1	3
3.	20 - 30	4	3	8	4	2	3
4.	30 - 40	2	_	6	2	1	5
5.	40 - 50	1	2	8		-	_
6.	50 - 60	1	-	4	@l _{max}	***	· · · · · ·
7.	7 60		- 1	4		_	
* * * * * * * * * * * * * * * * * * * *		-					
Total		31	13	32	16	7	15

S = Superficial burn

D = Deep burn

M = Mixed burn (both superficial & deep burn).

TABLE - V

Showing surface culture reports.

				PVP	z +			The continue of the continue o				Filler	77.70	Amniotic Membrane	707			
Organism	100	orf ;	Superficial		Deen			M	Mixed	Sui	erfi	Superficial	Н	Deep			Mixed	- 1
	1	2	3	-	2	8	1	2	3	1-1	2	E)	Н	2	3	1	2	1
				- 1				-	-									
Staphylococcus	16	0	ഗ	ω	4	~	12	ഹ	m ·	9	7	m	4	4	m	ω .	ហ	
Streptococcus	9	4	٠ ط	ന	1	1	ω,	ო		2	т	Ī.	1	ı	1	0	Н	
Escherichia coli	ω	Ŋ	-	9	Н	1	12	Ω	, ←	7	स्न	. t	2	ન	Н	7	₩.	
Klebsiella	4	rel		4	2	2	9	m	, 1	~	1 -	1	 1	1	ı	7	₩-	
Proteus	ω	Ω.	7	2	73	1	Φ	4	1	r-i	ľ	ı	ı	1		, , - 	99	
Pseudomomes	10	4	m	4	2	. 1	4	- 8	Н	10	4	7	~ ~	·	↤	ω	4	

l = At the time of admission

2 = 7th day post burn

3 = 18th day post burn.

49

TABLE - VI

Bacterial count after treatment.

ane	18th day D M Total	*	6 17 44.73%	7 16 42.10%	2 5 13.15%
Membr			2	m	2
ic	က		- 6	9	~ ~
Amniotic Membrane	Total		14 36.84%	18 47.36%	18.42%
) - ,	7th day D M		4	7	rU
	7±]		0 - -	4	7
	Ŋ		σ · · · · · · · · · · · · · · · · · · ·	r-	1
	day Total	A-	52 68.42%	23 30.26%	2.63%
	18th day M To		21	10	H
Z	Ω		52	9 4	H 1.
+ dAd	7th day	- 1	40 52.63%	14 5 14 33 43.42%	1 3 5 6.57%
	th d		16 7 17	44	m
	10	2	7	Ŋ	ન
	0	2	16	다 작	ન
	Bacterial count		Sterile	_10 ⁵ /cm²	710 ⁵ /cm ²

S = Superficial burn,

D = Deep burn,

M = Mixed burn (both superficial & deep burn).

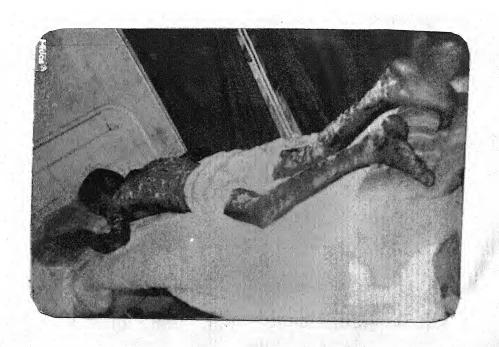
 $\frac{\text{TABLE - VII (a)}}{\text{Rate of healing with PVP + N}}.$

Healing time	PARTITION OF THE PARTIT		Pero	PVP +		irn		
(days)	0-10	10-20		-		50-60	760	Total
Superficial		*			-			
0 - 15	15	8	3	2,	-	-	_	28
16 - 30	-	_	1		1	1	_	3
31 - 45	·	_	-	-			<u> </u>	-
46 - 60	99000		****	_		-		-
7 60	-	-		_		_	-	_
		MICH MANN MARCH	*****	-	andres sylver business	****	-	un thurse hydren arbeiteur
Deep								
0 - 15	2	,	-	-		-	-	2
16 - 30	3	2	1		1	-		7
31 - 45	•	-	_	-	1			1
46 - 60		_	3	-	-	_	· parties	3
7 60	-	-	-	-			_	
				-	1400 COOK STORE		-	ne second solder solder
Mixed								
0 - 15	* = = * =		-		1	-	-	1
16 - 30	_	2	2	1	nim	1	1	7
31 - 45	_	-	4	4	5	2	-	15
46 - 60	<u> </u>	-	1	1	1		-	3
7 60	100	-		V ₁ , 2, 7,	1 -	3	2	6

TABLE - VII (b)

Rate of healing with Amniotic Membrane.

			. Ar	nniotic	Membi	ane		
Healing time (days)			Per	ccentag	ge of	burn	7.00	Total
(days)	0-10	10-20	20-30	30-40	40-50	50-60	/60	Totar
Superficial	*	•						
0 - 15	2	-	-		1000	_	,	2
16 - 30	3	1	1	1.		_	-	6
31 - 45	2	ż	3	me.		****	***	7
46 - 60	-	*****	***	1	•	-	entit	1
7 60		-	eme	***	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	*		_
man myst steam steam steam state		-	man samen salesta ad		DEF ANGEN MATERIAL DATA	-	-	-
Deep								
0 - 15	1	_		***************************************			-	1
16 - 30	2	1	1	-	_	-	-	4
31 - 45	_	_	1	1	-	-	· · · · · · · ·	2
46 - 60	_		-	_	-	- +,		-
7 60	•	w <u>-</u>	-		_		-	- \
								-
Mixed								
0 - 15	1	-	-	-	-	naken.		1
16 - 30	2	1	2	-	-	-		5
31 - 45	1	2		1		-		. 4
46 - 60			1	2	•	-		3
7 60				2	-	-		



Photograph No. 1

Showing healing after 18th day of application of Betadine and Neosporin powder.



Photograph No. 2

Same patient as in Photograph No. 1 showing complete healing on 30th day.





Photograph No. 3

Showing progressive healing after 18th day of application of Betadine and Neosporin powder in deep burn patient.



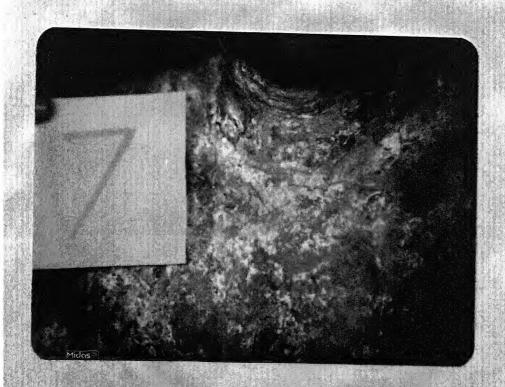
Photograph No. 4

Showing healing after 10th day of application of Betadine and Neosporin powder in superficial burn patient.



Photograph No. 5

Showing healing and early escharolysis after 10th day of application of Betadine and Neosporin powder.



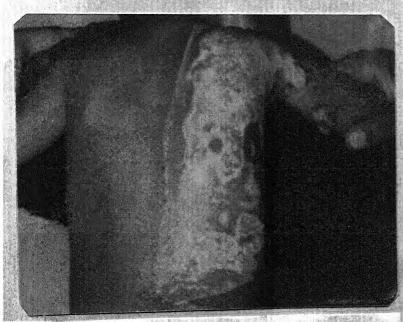
Photograph No. 6

Showing healing after 7th day of application of Betadine and Neosporin powder in superficial burn patient.



Photograph No. 7

Showing healing after 7th day of application of Betadine and Neosporin powder.



Photograph No. 8

Showing immediate application of Amniotic membrane over cleaned burn area.



Photograph No. 9
Showing progressive healing from the periphery on 20th day of membrane application.



Photograph No. 10
Showing complete healing after
30th day of membrane application.

DISCUSSION

ar our control of admired actions.

DISCUSSION

Local burn wound management is still in the phase of trial. After many advances in medical science, mortality from burn has definitely reduced, but morbidity from contracture and keloid are still crippling the sufferer physically, mentally as well as socially.

Burn gives rise to a wide raw area of variable degree of depth. In full thickness burns, the vascular thrombosis is confluent and involves arterioles, venules and capillaries, extravasated erythrocytes and oedema are present in extravascular tissue to a variable degree. These changes are not necessarily confined to the dermis but may extend into the subcutaneous part or beyond, depending on the severity of injury. The devitalized tissue (eschar) eventually will slough spontaneously, mostly as a result of bacterial enzymatic proteclytic action. This pabulum of denatured protein and cellular debris, which constitutes the eschar, provides a substrate for proliferation of micro-organisms. The more efficient the wound bacteriostasis, the longer will be required for slough to occur (Order, S.E., Moncrief, J.A., 1965; and William, W. Monafo et al, 1987).

In partial thickness burns, thrombosis is incomplete and in superficial injury is limited to the upper or papillary dermis. The dermal circulation is restored gradually in partial thickness burns, but the process requires several days or more, so that significant interval of relative ischemia is present. Even in more superficial burns sloughing of partial thickness eschars will occur spontaneously as epithelial elements spread from viable remnants of the skin appendages to cover the denuded dermal surface (Order, S.E., Moncrief, J.A., 1965 and William, W. Monafo, et al., 1987).

It is evident from the foregoing that the delivery of systemically administered antimicrobial agents to the burn wound is limited. It is the zone of stasis, produced by ischemia and necrosis of tissue, which limit and to a large degree negate the efficacy of systemically administered antibiotic directed at burn wound sepsis by forming an effective barrier, preventing medication from reaching the vital area of sepsis, namely the subescharotic area. The systemically administered antibiotic can only reach the ischemic area from gradient diffusion from wound periphery which is inadequate to prevent colonization.

(William, W.M., Bruce, F., 1987; Kock, D.M., 1985).

Many attempts have been made to limit the extent of the zone of stasis by such means as more effective

resuscitation, maximum dose of heparin and steroids, but all have proved unsuccessful. Clearly, the topical application of antimicrobials will be the best method to ensure that they are present in adequate concentrations, at least on the wound surface, where the risk of bacterial contamination is the greatest.

Normal skin contains a sparse microflora consisting mainly staphylococcus epidermidis, diphtheroids and other bacterial species that are not ordinarily highly virulent. Burn wound cultures taken within a few hours following injury typically yield few or even none of the normal flora unless there has been contamination, usually by soil or fetid water during rescue and transport. The rapidity with which subsequent colonization occurs and the microbial density that is reached eventually, depends on many factors, the most important of which are wound extent and depth and prior state of the patient's health. In untreated, extensive deep wounds, for example, dense colonization, primarily by gram positive cocci, often occurs within 24 hours. Within 3 to 7 days, aerobic gram negative bacteria particularly pseudomonas aeruginosa typically appear. Untreated this initial colonization gives way to confluent, deeper spread via the ducts of skin appendages. Ultimately active invasion of unburned subjacent tissue may occur and spread systemically leading to septicaemia. In burn of lesser extent, particularly

if they are relatively superficial, healing may occur spontaneously, but the danger of conversion of superficial burn to deep burn by infection and/or dissociation and loss of body constituents remain a major problem.

Therefore, adequate topical therapy should be initiated as rapidly as possible following injury, irrespective of the depth of burn (W. Monafo, & Bruce Freedman, 1987).

with better understanding of pathophysiology of burn wound, there is some consensus that wound infection is the primary source of morbidity and mortality from extensive burn injury. Therefore the main aim in the treatment of burn is to re-establish the continuity of skin. The raw area after burn should be covered to make it a closed wound which subsequently reduces excessive evaporative water loss and prevents wound infection (Demling, R.H., 1983).

Autograft skin grafting is the most accepted procedure for management of burn wounds. However, limited available skin donor sites preclude the achievement of prompt closure of burn wound (Bruke, J.F. et al, 1974). Alternatively various temporary measures such as allografts, heterografts or a variety of ingeneously engineered skin substitutes to protect the open burn wound have been and are being tested for this purpose (Park, G.B., 1978 and Burke, J.F., 1981). But to date

there is no evidence that mortality or morbidity - most of which is still because of infection - has been reduced in burns that exceed 40 percent of total body surface area, in addition these substitutes have limited availability and a very high cost. However, amniotic membrane has been used by various investigators and is still in use as a substitute for skin. The amniotic membrane fulfilled all the functions of an ideal biological dressing. In terms of their large size and readily availability at no cost to the patients. In addition, the membrane appears to have another property subjectively, the rapidity of ingrowth of epithelium from the borders of wound in full thickness defects and the rate of re-epithelization of partial thickness burns, appear to be increased by their use. Choao et al (1940) and Troensegard Hansen (1950) also have noted that amniotic membrane seemed to possess some specific healing power. They have reported a stimulation of both fibrous tissue growth and more rapid epithelial repair. Thus it is logical to compare the effectiveness of the combination of topical PVP solution + Neosporin powder and amniotic membrane as topical burn therapy.

Local polymyxin + Neomycin + Bacitracin (Neosporin) and Povidone iodine (PVP) combination forms an almost complete barrier against microbials. Polymyxin can protect the burn wound against colonization by Pseudomonas

pyocyanea, but not so against staphylococcus aureus and haemolytic streptococci. Povidone iodine on the other hand has wide antibacterial, antifungal, sporicidal and viricidal properties. Neomycin and Bacitracin supplement this action especially in relation to gram negative organisms.

Burn wound biopsy provides quantitative and qualitative bacteriology. Bacterial counts less than 10⁵/cm² of tissue exclude burn wound sepsis. If on the other hand the number of bacteria is more than 105/cm2 of tissue wound sepsis is generally present. There is correlation between death rate and presence of burn wound sepsis. No death occurred in patients, whose wounds biopsies revealed $\angle 10^5/\text{cm}^2$ of tissue, and patients died from burn wound sepsis, their wound biopsies showed 710⁵ bacteria/cm² of tissue (Artz, Moncrief & Pruitt, 1979; Berset & Chiolero, 1982; Krupp, 1982; Zamora, 1984 and Zelluer, 1980). Our study using PVP + N showed an appreciably better percentage of sterile cultures as compared with Amniotic membrane, both at seven days (52.6% vs 36.8%) and 18 days (68.4% vs 44.7%). Similarly, the numbers of cultures below $10^5/\text{cm}^2$ were significantly less for PVP + N both at 7th and 18th days (43.4% & 30.2% vs 47.3% & 42.1%). Even patients with a count of more than 105/cm2 were less in group treated with PVP + N (6.5% & 2.6% vs 18.4% & 13.2%). These figures agree with other studies. Thus Moncrief has shown 49% sterile

cultures and 84% less than the critical level of $10^5/\text{cm}^2$ in a study of more than 3200 bacterial cultures which compare well with our corresponding values of 68.4% and 30.2% on day 18, using PVP + N. Zellner and Bugi (1985) too have shown better results with PVP as compared to amniotic membrane. Our results which are markedly better than other studies with only PVP are due to the addition of neosporin.

The role of healing also showed a marked improvement on amniotic membrane in superficial, deep and mixed burn categories. The tanning effect of PVP is an added advantage for this keeps the surface dry, so holding colonization to a low level and also permitting early surgery. PVP + N combination forms a 'crust' which sets up a barrier to colonization and at the same time keeps the surface dry. In patients with superficial burns when epithelization was complete the crust separated itself and in clean cases no single incidence of infection was found.

In deep burn wounds, multiple injections of PVP subescharaly helped in two ways. In the first place, it kept the subescharal count to a low level. In fact this bacterial colonization and its inaccessibility to topical bacterial colonization and its inaccessibility to topical antimicrobials have been major factors in burn wound sepsis of deep burns. That subescharal injection of PVP was

beneficial and evident from the results, namely no single septicaemic mortality occurred in deep burn patients.

The second beneficial effect is that it opens up sub-escharal plane thus helping in early escharolysis and decreasing bleeding on separation.

The burn wound in most of these patients could be grafted immediately after the eschar separation which was in marked contrast to the fact that topical agents are totally ineffective in subescharal colonization including superficially applied PVP cream and also that after escharectomy or lysis a considerable period of time is spent in limiting the infection at the burn site, before grafting can be taken up. Subescharal PVP injections were attempted basically because PVP has been shown to have beneficial antibacterial effects when used subcutaneously, intrapleurally or intraperitoneally without any serious iodine toxicity. The concentration of 0.25% PVP may seem to be too low for it to be effective but it has been mentioned that with this concentration there is an increase in free iodine and antibacterial activity. None of our patients showed any clinical evidence of iodine toxicity. The PVP injections in deep burns of more than 50% were limited to three in order to limit the total amount of PVP injected. We found that subescharal injections markedly reduce the incidence of septicaemia and mortality in these patients and at the same time keep

the surface healthy. Application of PVP + N was accompanied by minor pain. Once 'crust' has been formed, pain disappeared. Pain was not accompanied with application of Amniotic membrane, but submembranal suppuration causes great discomfort to the patients since it is a closed dressing. PVP was an open method and did not require removal of previously applied layer, and being an open method there was no question of suppuration being collected at any site. This in our view is an important psychological and clinical advantage and at the same time saves a lot of nursing personnel time. The iodine level are elevated after PVP application but this level creates no significant impairment of thyroid functions or manifestations of iodine toxicity. Further, the iodine levels returns to normal within a week after applications are stopped. Similarly the repeated serum creatinine compared with those of patients being treated with amniotic membrane showed that no toxicity because of drugs contained in neosporin mainly bacitracin and neomycin sulphate which are renally toxic. This was probably because after the three and two applications were limited to only those areas which were denuded, thus largely limiting the total amount of drugs used to a bare minimum. Even the PVP solution used, compared favourably with PVP ointment, commonly used, in terms of lesser amount of PVP used.

CONCLUSION

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CONCLUSION

The comparative effects of PVP solution +
Neosporin powder and amniotic membrane application
were studied and compared in 114 patients, out of which
47 patients were of superficial burn, 20 patients with
deep burn and 47 patients with mixed burn. At the same
time superiority of either of them was observed. The
conclusions drawn were as follows:

- Females are more commonly burnt than males, for they are exposed to this danger due to house work.
- 2. The incidence of burn is much higher in younger age-group, i.e. below 30 years of age.
- 3. Most of the burns are thermal in nature.
- 4. Superficial and mixed burns are more common than deep burns.
- 5. Burn involving smaller areas, irrespective of their depth of burn, healed quickly and with an cosmetically acceptable scar.
- No allergic reaction were observed in both types of dressing.

- 7. Contracture were observed in one case when treated with PVP + Neosporin powder, while 2 cases were observed with Amniotic membrane treated patients.
- 8. Period of hospital stay was shorter in PVP + Neosporin powder treated patients.
- 9. The scars were brownish tinged, hyperpigmented and had a flat margin and were more fibrous in PVP + Neosporin powder treated patients while completely healed area were pink and had a flat margin in amniotic membrane treated cases.

On comparing the effect of two dressing to assess the superiority of either of them, following conclusions were drawn.

- Both the dressing materials were easily available and were easy to apply.
- 2. Povidone iodine with neosporin powder requires no specific storage facilities while amniotic membrane requires storage in sterile container with saline dilution in 1: 40 at 4°C with addition of Kanamycin or 10 lakhs units of crystalline penicilline or 1 gm. of streptomycine sulphate etc.

- 3. Application of PVP + Neosporin powder was accompanied by minor pain, but once crust has been formed, the pain disappears and was not observed on further applications of PVP + Neosporin powder, while application of amniotic membrane cause no pain to patients except during cleaning.
- 4. No suppuration was seen in patients treated with PVP + Neosporin powder, because it is an open method of dressing. Sub-membrane suppuration was observed with application of amniotic membrane which caused great discomfort to the patients.
- 5. The healing rate is faster in patients treated with PVP + Neosporin powder as compared to patients treated with Amniotic membrane.
- 6. The amniotic membrane gave good results with superficial burns, while PVP + Neosporin powder gave good results with all type of burns.
- 7. Povidone iodine lotion injection, diluted in saline injected in subescharal plane gave very good results in controlling infection and early escharolysis, followed by early grafting and higher rate of take-up and subsequent healing and thus reduced chances of septicaemia.

In brief, the conclusion may be drawn that treating all types of burn patients by using PVP + Neosporin powder is markedly superior to ammiotic membrane application as shown by minimal infection rate and markedly reduced healing time. This is basically because of wide spectrum action, tanning effect of PVP and attainment of dry surface.

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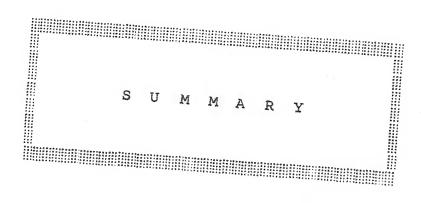
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SUMMARY

Improvement in infusion therapy in burn has led to reduction in mortality due to acute shock. But management of burn wound sepsis is still a very challenging problem in terms of morbidity and mortality, in spite of vast advances in medical sciences and availability of various broad spectrum antibiotics.

Many treatment modalities have been advocated by various workers from time to time so far, but all have their own advantages and disadvantages. Of course, autogenous skin grafting after early excision of burn wound is the best covering material amongst all suggested till now. But it has its own limitations in terms of limited availability, unfitness of already shocked patients for surgical procedure involved in skin grafting and subgraft suppuration.

Fortunately enough more comprehensive knowledge is now available about the pathophysiological changes that accompany the major thermal injury. The avascular nature of burn tissue as a result of thrombosis of vessels, wound maceration and necrosis limit the delivery of systemically administered antibiotics and favour

microbials proliferation which provides the local source of virulent organism leading to frank septicaemia and death.

Thus, it is necessary that treatment of local infection be given priority and since systemic delivery is sub-optimal, more reliance is to be put on local method of control of infection. Because of the inadequacy of presently used local application we needed to re-examine a new combination of locally applied chemotherapeutics/ antibiotics.

The topical agent should be antiseptic, nonantigenic, non-toxic systemically or locally and local
analgesic effect is also desirable. It should minimize
the vaporizational heat loss and of course should be of
low cost.

The present work was undertaken and designed to compare the efficacy of topical PVP + Neosporin and Amniotic membrane and at the same time to assess the supremacy of either of them. A total of 114 patients were kept in this study. Out of which, 53 were male patients and 61 were females. Most of the patients belong to younger age group.

Out of 114 patients, three groups of patients were made, namely 47 patients with superficial burns in

Ist group, 20 patients with deep burns in IInd group and 47 patients with mixed burns (both superficial & deep burns) in IIIrd group. Each group was sub-divided into two sub-groups. One sub-group was treated with PVP + Neosporin and another by application of Amniotic membrane.

Application of both dressings was done after prior cleaning by 1% Savlon and sterile saline. The first sub-group of patient treated with sprinkling of Neosporin powder to form a uniform layer with 1% available iodine which was sprayed uniformly, thus completely soaking the powder. A further layer of powder was applied to form a crust. On first day, three applications were carried out without removing previously applied layers. On second day the applications were reduced to two and from third day onwards this application was limited to those area from which the crust was either separated or cracked. patients with deep burns, apart from application of PVP + Neosporin, injection of 0.25% iodine in subescharal plane at multiple sites were given on third post-burn day and repeated twice weekly until escharolysis was completed. Second sub-group of patients treated with application of Amniotic membrane and no dressing was applied because wound remained closed.

There was minimum incidence of infection in PVP + Neosporin treated patients as shown by culture and wound biopsies reports as compared to Amniotic membrane treated patients. There was higher incidence of submembrane suppuration as compared to patients treated with PVP + Neosporin.

As for rate of healing, most of the superficial burn patients, when treated with PVP + N showed complete healing within 15 days while amniotic membrane sub-group, majority healed within 30 days, a substantial number of wound took 45 days to heal. Deep burn patients treated with PVP + N required 45 days for complete healing and few wound took more than 45 days, while Amniotic membrane treated patients showed complete healing within 45 days (percentage of burn was less in this sub-group as compared to PVP + N treated sub-group). Sub-group of mixed burn patients treated with PVP + N showed complete healing within 45 days. Few patients required more than 60 days as their percentage of burn was varies from 40-60%. Patients of this group treated with Amniotic membrane took 45 days for complete healing while substantial number of patients required more than 60 days. At the same time, the subescharal injections of PVP in deep burn patients showed a distinct reduced septicaemia and local infection rates, early escharolysis followed by early graft take-up and subsequent healing.

Comparing the two dressings, it was concluded that -

- Both the dressings are easily available and easy to apply.
- 2. There was no significant allergic reaction noticed with both types of dressing.
- 3. The healing is faster in Povidone iodine with Neosporin powder treated patients than Amniotic membrane treated patients.
- 4. Incidence of infection is more in Amniotic membrane treated patients than PVP + Neosporin powder treated patients.

Povidone iodine + Neosporin powder gave better results than Amniotic membrane application.
